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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| MAIER, LEIGH C | |
| **ART UNIT** | **PAPER NUMBER** |
| 1623 | |

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/625,645 | CHRISTIAN ET AL. | |
| | Examiner | Art Unit | |
| | Leigh C. Maier | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) *1-38,63-65 and 67-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-62, 66, and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

In the response the restriction requirement, filed August 22, 2006, Applicant has proposed two new groups, Group V (claims 39-62) and Group VI (claims 63-75), and has provisionally elected Group V. The examiner accepts this new group and considers it to be essentially* a sub-genus of claim 1 in Group I. However, the examiner does not agree with the inclusion of the compounds recited in claims 66 and 75 in Group VI. These appear to be encompassed in the structural formula of claim 39, regardless of their method of preparation. They are therefore included in the claims under examination. Method claims 56, 57, 59 and 60 are also included because the compounds of claims 55 and 58 are allowable, so their methods would be subject to rejoinder anyway.

*It is noted that because of the discrepancy in the definition of $R_2$ in claim 1 and claim 39, Group V is not strictly encompassed by claim 1. It is the opinion of the examiner that the new definition of $R_2$ in newly submitted claim 39 introduces new matter (discussed below) into the claim. If claim 39 is amended so that the definition of this variable is the same as claim 1, the search may be expanded to other species in claim 1.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-43, 45-51, 53 and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that Applicant, at the time the application was filed, had possession of the claimed invention. The variable $R_2$ is defined as set forth in section e) of claim 39. However, the examiner finds no support for a definition other than hydroxyl for this variable in the present specification. Neither is such a definition supported by any of the applications to which Applicant claims priority.

Claims 39-54, 61, 62, 66 and 75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds having two hydroxyls as the maximum number of (non-hydrogen) substituents on the phenyl ring and a hexose as the saccharide moiety, does not reasonably provide enablement for the full scope of the compounds defined by the structural formula set forth in claim 39. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims without undue experimentation.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);
(2) The amount of direction or guidance presented;
(3) The presence or absence of working examples of the invention;
(4) The nature of the invention;
(5) The state of the prior art;
(6) The relative skill of those in the art;
(7) The predictability or unpredictability of the art; and
(8) The breadth of the claims.

The claims are drawn to compounds described as doparminergenic prodrugs that are able to traverse the blood-brain barrier via a glucose transporter. Therefore, the compounds' efficacy depends on their interaction with dopamine receptors, transporters and glucose transporters, particularly GLUT1 and GLUT3. However, these receptors/transporters are known to have particular structural requirements.

Taking the "dopamine" portion of the molecule first, it is known that slight variations in the dopamine structure have a large impact on its interaction with the transporter and receptor. See Meiergerd et al (J. Neurochem., 1994) at abstract; Table 3; and Figure 3. See also, Knoerzer et al (J. Med. Chem., 1994) at Figure 4. Although, there appears to be some room for variations in variables $R_5$ and $R_6$, due to steric considerations, it appears unlikely that further substitution on the phenyl ring would allow for necessary binding. Furthermore, in a post-filing publication, Jiang et al (Clin. Neuropharmacol., 2004) acknowledges the "stringent structural requirements at D1 and D2 receptors and at DAT [dopamine transporter]." See page 64 at first full paragraph. Although the structural requirements for dopamine receptors and transporters are known and apparently somewhat predictable, the claims are drawn to a broad range of compounds, *most* of which appear to have little or no chance of being recognized by or binding to these entities.

With respect to the glucose transporter, it is known that glucose transporters (generically termed *hexose* transporters) can transport drugs across the BBB. See Tamai et al (J. Pharm. Sci., 2000) at the section bridging pages 1376 and 1377. Even among hexoses, there are great differences in transportability with GLUT3, for example. See Maher et al (Biochem. J., 1996) at Table 1. There is no indication that these hexose transporters would recognize anything other than C6 monosaccharides. However, the instant compounds encompass a saccharide entity that

may be C3 to C9. It is further noted that the variation in these monosaccharides is much more broad than the carbon number would suggest because of the great variety of compounds within each carbon number. For example, a C5 monosaccharide, would encompass many pentoses. Although a C5 monosaccharide derivative is prepared, the examiner finds no evidence of testing or efficacy for this compound.

It appears that the testing is limited to compounds that would be expected to interact positively with the appropriate receptors and transporters. Although the level of skill in this art would be expected to be high, and some number of inoperable embodiments is permissible in an enabled invention, it appears from what is known regarding structural requirements, discussed above, that the bulk of the embodiments would be inoperative. Therefore, one of ordinary skill would require undue experimentation in order to use the compounds for their described utility commensurate with the scope of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39 and 41-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Section h) of claim 39 recites "N is the nitrogen atom of a primary or secondary amine or an amide." By definition, a primary amine has exactly two hydrogen substituents. Also by definition, the nitrogen atom in the structural formula has no more than one hydrogen substituent. These conflicting limitations render the claims vague and indefinite.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39, 41, 43, 46, 47 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Ovalle et al (Carbohyd. Res., 2000).

Ovalle discloses the compound glucitol-*N*-TBT, which is consistent with the structural formula of claim 39. See Table 1.

Claims 39, 41-43, 46, 47 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Wunder et al (Int. J. Oncol., 1997).

Wunder discloses a compound consistent with the structural formula of claim 39. See Caplus abstract.

Claims 39, 41-43, 46, 47 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohnishi et al (J. Drug. Targetting, 2000).

Ohnishi discloses a compound consistent with the structural formula of claim 39. See Caplus abstract.

Claims 39, 41-43 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Tarjanyi et al (New Approaches Chromatog., 1993).

Tarjanyi discloses a compound consistent with the structural formula of claim 39. See Caplus abstract.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 39-55, 58, 61, 62, 66 and 75 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 6,548,484. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claim does not particularly define the non-saccharide portion of the molecule. However, the written description of the invention includes species that anticipate the instant invention. See example. One of ordinary skill would be motivated to select these species, thus making the instant invention obvious.

***Allowable Subject Matter***

Claims 55-60, although subject to an obvious-type double patenting rejection, appear to be free of the art. The following is a statement of reasons for the indication of allowable subject matter: Both of Nakada et al (US 5,380,837) and Fernandez et al (Carbohyd. Res., 2000) disclose the preparation of glycosyl dopamine derivatives. See Nakada at col 9-10. See Fernandez at Scheme 1. Neither of these references teach or fairly suggest the allowable subject matter.

***Examiner's hours, phone & fax numbers***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
November 10, 2006